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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
HUTSON, RICHARD G	

ART UNIT	PAPER NUMBER
1652	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/821,583	WANG ET AL.	
	Examiner	Art Unit	
	Richard G. Hutson	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 March 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-26* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-26* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's amendment of claims 1-14 and the addition of new claims 15-26, in the paper of 11/28/2007, is acknowledged. Claims 1-26 are at issue and are present for examination.

Applicants' arguments filed on 11/28/2007 and 3/26/2008, have been fully considered and are deemed to be persuasive to overcome some of the rejections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

Claim Objections

Claims 16, 19 and 25 are objected to because of the following informalities:

Claims 16, 19 and 25 are missing a period at the end of the claim.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-26 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to

reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

This rejection was stated in the previous office action as it applied to previous claims 1-14. In response to the rejection applicant's amended claims 1-14 and added new claims 15-26 and traverse the rejection as it applies to the newly amended claims.

Applicants submit that the standard for written description is that one of skill must demonstrate possession of the claimed invention and f a genus, this can be achieved by description of representative species or providing general structural characteristics in combination with function. Applicants submit that the specification provides such description in that applicants have disclosed any number of polymerases that can be modified using a nucleic acid binding domain as claimed, for example, Taq polymerase.

Applicants further submit that the specification not only fully describes polymerases for use in the invention, but also provides description of Sso7d nucleic acid binding domains as recited in the claims, such as the structural feature of the genus of Sso7d proteins for use in the invention, *i.e.,* reference SEQ ID NO:2, and provides structural and functional characteristics of proteins encompassed by the genus. Applicants further submit that the specification further describes references that disclose other Sso7d homologs and describes structural analyses of Sso7d and Sac7d when bound to DNA. Applicants submit that the application also teaches that this DNA binding function can be used as a basis for selecting DNA binding domains that can be used to enhance polymerase processivity.

Applicant's amendment of the claims and applicants complete argument are acknowledged and has been carefully considered, however, are found nonpersuasive for the reasons previously made of record and repeated herein.

With respect to applicants submission that the specification provides adequate description as per the statue, in that applicants have disclosed any number of polymerases that can be modified using a nucleic acid binding domain as claimed, it is pointed out to applicants that while applicants do list a number of polymerases as a number of polymerases are known, applicants only teach that two, Delta Taq and Pfu DNA polymerase, of the many known polymerases are able to have their processivity enhanced as a result of the joining of a double stranded nucleic acid binding domain.

With respect to applicants submission that the specification also provides description of Sso7d nucleic acid binding domains as recited in the claims, such as the structural feature of the genus of Sso7d proteins for use in the invention, *i.e.,* reference SEQ ID NO:2, and provides structural and functional characteristics of proteins encompassed by the genus it is noted that applicants provide the protein of Sso7d comprising the amino acid sequence of SEQ ID NO:2, and teach this protein joined to either Delta Taq or Pfu DNA polymerase, however, applicants do not describe any other species of the claimed genus or describe this double stranded nucleic acid binding domain joined to any other polymerase domains. While homologs of the Sso7d protein may be known, it is not shown or clear that these homologs would have the same interaction with all polymerase domains.

Given this lack of additional representative species as encompassed by the claims, applicants have failed to sufficiently describe the claimed invention, in such full, clear, concise, and exact terms that a skilled artisan would recognize Applicants were in possession of the claimed invention.

Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

Claims 1-26 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for those methods of amplifying a target nucleic acid, comprising the use of a protein comprising two heterologous domains, wherein the first domain is a sequence-non-specific-double-stranded nucleic acid-binding domain joined to a second domain which is a Taq or Pfu DNA polymerase domain, wherein said sequence-non-specific-double-stranded nucleic acid-binding domain is Sso7d comprising the amino acid sequence of SEQ ID NO: 2, does not reasonably provide enablement for any method of amplifying a target nucleic acid, comprising the use of a protein comprising two heterologous domains wherein the first domain is a sequence-non-specific-double-stranded nucleic–acid-binding domain joined to a second domain which is any polymerase domain, wherein the first domain is any sequence-non-specific-double-stranded nucleic acid-binding domain wherein said domain specifically binds to any polyclonal antibody generated against Sso7d, joined to any polymerase domain. The specification does not enable any person skilled in the art to which it

pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

This rejection was stated in the previous office action as it applied to previous claims 1-14. In response to the rejection applicant's amended claims 1-14 and added new claims 15-26 and traverse the rejection as it applies to the newly amended claims.

As above, applicants submit that the specification provides multiple examples of enhancement of processivity of polymerases using Sso7d and its homologs. Applicants submit that in addition to the general guidance regarding polymerases and Sso7d proteins provided by the specification, the examples provide data for four exemplary embodiments using two Sso7 proteins (Sso7d and Sac7d) and three polymerases (Taq, Delta-Taq, and Pfu). Applicants submit that these data provide further evidence that the claims are enabled.

Applicants have also provided a Declaration under 37 C.F.R. § 1.132 by Peter Vander Horn ("the Vander Horn Declaration") in the parent application and Applicants respectfully request that the Declaration, a copy of which is enclosed, be made of record in the instant application, as the same issues are being raised. Applicants submit that the Vander Horn Declaration provides objective reasons further justifying the claimed genus of methods.

Applicants submit that the Sso7d nucleic acid binding domains set forth in the claims are not derived from a novel gene and a natural variation of about 76% occurs within the family (as noted in the Vander Horn Declaration, which is discussed in greater

detail below). Applicants submit that Analyses of the structures of Sso7d and Sac7d bound to DNA have been performed by several investigators and the specification directs a practitioner to exemplary references describing such studies .

Applicants submit that Similar x-ray crystallographic analysis has also been performed for the related protein Sac7d *(e.g.,* Robinson, *et al., Nature* 392:202-205, 1998, which reference is cited by Gao *et al.) and* Gao *et al.* additionally compare the Sso7d-DNA complex to the Sac7d-DNA complex. Thus, the specification therefore properly enables the claimed methods. Applicants submit that they have provided objective reasons justifying the percent identity set forth in the claims. Applicants submit that not only does the subject specification provide a full disclosure of the family of Sso7 proteins, Applicants have provided the Vander Horn declaration, which provides objective reasons justifying the 75% level of identity recited in the claims. Applicants submit that Dr. Vander Horn explains that by following the differences between the family members, those of skill would immediately recognize where the critical and noncritical regions of the proteins are located and Applicants submit that as Dr. Vander Horn notes in his Declaration, to limit the claims to a percentage above that found within the naturally occurring variants is to ignore that nature has provided this road map for introducing mutations.

Applicants further submit that in addition to the natural variations between family members, any competent protein chemist readily understands that non-naturally occurring but conserved substitutions are possible throughout the primary sequences of

the prototype proteins as Dr. Vander Horn explains this conventional wisdom at section 9 of his Declaration.

Applicants submit that furthermore, Dr. Vander Horn explains at section 10 of his Declaration that the structural features of the Archaeal protein interaction with DNA had been previously studied by workers such as Gao *et al.* Dr Vander Horn details how this information permits a practitioner to identify the critical binding domains in the proteins, which allows one of skill to focus mutations away from these critical regions so that amino acid residues may be substituted without compromising activity.

Applicants submit that the Vander Horn Declaration thus further illustrates how one of skill in the art can use the large body of knowledge in the art to identify functional Sso7d variants having the percent identity set forth in the claims without undue experimentation.

In view of the foregoing, the application provides proper guidance such that one of skill can identify a nucleic acid binding domain as claimed and that use it to modify polymerase processivity with a reasonable expectation of success.

Applicant's amendment of the claims and applicants complete argument are acknowledged and has been carefully considered, however, are found nonpersuasive for the reasons previously made of record and repeated herein.

As above, with respect to applicants submission that the specification provides multiple examples of enhancement of processivity of polymerases using Sso7d and its homologs, the provided examples, using two Sso7 proteins (Sso7d and Sac7d) and

three polymerases (Taq, Delta-Taq, and Pfu) are insufficient to enable the breadth of the claimed genus of methods of amplifying a target nucleic acid comprising the use of any sequence-non-specific double-stranded nucleic-acid-binding domain that comprises an amino acid sequence that has a mere 75% identity to the amino acid sequence of SEQ ID NO:2 and is joined to any polymerase domain with error-correcting activity, where the sequence non-specific double-stranded nucleic-acid-binding domain enhances the processivity of the polymerase domain compared to an identical polymerase domain not having the sequence non-specific double-stranded nucleic acid binding domain.

The complete declaration of Dr. Vander Horn is acknowledged and has been carefully considered.

It is appreciated that with regard to naturally occurring 7kDa proteins in the family of Archael DNA-binding proteins there are many family members reported in the literature and these are evolutionarily related allowing for mutations in these domains to be made while conserving the double stranded DNA binding ability.

While it is recognized that the art provides knowledge as to a great number of polymerases and additionally knowledge regarding the DNA binding domain of Sso7d and related homologs, it is the lack of teaching and knowledge of the interaction between the various polymerases as encompassed by the claimed methods and the ability of Sso7d homologs to increase the processivity of a polymerase domain that is key to applicants claimed invention. It is the knowledge and guidance related to this

relationship and interaction between the two different domains that is absent in the art and applicants specification. For this reasons applicants have not sufficiently enabled the breadth of the claimed genus of methods comprising the use of a protein comprising two heterologous domains wherein the first domain is a sequence-non-specific-double-stranded nucleic–acid-binding domain joined to a second domain which is any polymerase domain, wherein the first domain is any sequence-non-specific-double-stranded nucleic acid-binding domain wherein said domain specifically binds to any polyclonal antibody generated against Sso7d, joined to any polymerase domain

As stated previously and above, with regard to applicants submission that the Sso7d nucleic acid binding domains set forth in the claims are not derived from a novel gene and a natural variation of about 76% occurs within the family (as discussed in the Vander Horn Declaration) this variation within the family of proteins does not offer sufficient guidance as to those necessary features that result in the claimed increase in processivity of a joined DNA polymerase domain. It is likely that this complex interaction is a result of factors of both the double stranded nucleic acid binding domain as well as the specific polymerase domain itself. Applicants have not addressed this interaction.

In view of the foregoing, the application provides insufficient guidance such that one of skill could not identify those nucleic acid binding domains encompassed in the claims and use it to modify any polymerase domain's processivity with a reasonable expectation of success. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without

sufficient guidance, determination of those proteins and methods of their use having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-26 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 11, 15-19 and 22 of copending Application No. 10/306,827. Although the conflicting claims are not identical, they are not patentably distinct from each other because claims 11, 15-19 and 22 of 10/306,827 drawn to a method of increasing the yield of from a polymerase reaction on a target sequence comprising contacting the target nucleic acid with a polymerase joined to a sequence non-specific-nucleic –acid-binding domain anticipate claims 1-14 drawn to a method of amplifying a target nucleic acid, comprising the use of

a protein comprising two heterologous domains wherein the first domain is a sequence-non-specific-double-stranded nucleic–acid-binding domain joined to a second domain which is a DNA polymerase domain, wherein the first domain is any sequence-non-specific-double-stranded nucleic–acid-binding domain wherein said domain specifically binds to any polyclonal antibody generated against Sso7d, joined to any DNA polymerase domain.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Applicant's acknowledgement of this provisional rejection and statement that they will consider the filing of a terminal disclaimer to obviate the rejection is acknowledged.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Richard G. Hutson whose telephone number is 571-272-0930. The examiner can normally be reached on M-F, 7:00-4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Nashaat T. Nashed can be reached on 571-272-0934. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

rgh
8/15/2008

/Richard G Hutson, Ph.D./
Primary Examiner, Art Unit 1652